

IN THE SPECIFICATION

The Descriptive Title of the Invention has been amended as follows:

Method of Manufacturing a Stent Coating For Increasing Blood Flow to Ischemic Tissues
and a Method of Using the ~~Same~~Stent

Please insert the following section before the "**BACKGROUND OF THE INVENTION**" section beginning on page 1:

CROSS REFERENCE

This is a divisional application of U.S. Serial Number 09/846,498, which was filed on April 30, 2001.

Paragraph 24 beginning on page 7 has been amended as follows:

[0024] TGF-beta exists in at least five isoforms, each of which is encoded by a different gene. TGF-beta directly induces proliferation, migration and/or differentiation of endothelial cells. It has been reported that TGF-beta signaling may regulate VEGF expression in cardiac myocytes. (Zheng[[,]] et al., "Mechanisms of coronary angiogenesis in response to stretch: role of VEGF and TGF-beta," Am. J. Physiol. Heart Circ. Physiol., 280(2):H909-17 (February 2001)[[.]]).

Paragraph 28 beginning on page 8 has been amended as follows:

[0028] PR39, a macrophage-derived peptide, inhibits the ubiquitin-proteasome-dependent degradation of HIF-1-alpha protein, resulting in accelerated formation of vascular structures in vitro and increased myocardial vasculature in mice. Coronary flow studies in mice have demonstrated that PR39-induced angiogenesis resulted in the production of functional blood vessels. Such findings indicate that PR39 and related compounds can be used as potent inductors

of angiogenesis and that selective inhibition of HIF-1- α degradation may underlie the mechanism of inflammation-induced angiogenesis. (Li[[,]] et al., "A peptide regulator of angiogenesis," *Nat. Med.* 6(1), 6(3), pgs. 49-55 (January and March 2000)).

Paragraph 29 beginning on page 8 has been amended as follows:

[0029] Del 1, an extracellular matrix protein, encodes three Notch-like epidermal growth factor repeats: an RGD motif, and two discoidin domains. Del 1 is expressed in an endothelial cell-restricted pattern during early development. In some studies, recombinant baculovirus Del 1 protein was shown to promote α v β 3-dependent endothelial cell attachment and migration. Attachment of endothelial cells to Del 1 was associated with clustering of α v β 3, the formation of focal complexes, and recruitment of talin and vinculin into these complexes. These events were shown to be associated with phosphorylation of proteins in the focal complexes, including the time-dependent phosphorylation of p125(FAK), MAPK, and Shc. When recombinant Del 1 was evaluated in an in-ovo chick chorioallantoic membrane assay, it was found to have potent angiogenic activity. This angiogenic activity was inhibited by a monoclonal antibody directed against α v β 3, and an RAD mutant Del 1 protein was inactive. Thus, Del 1 has been indicated to provide a unique autocrine angiogenic pathway for the embryonic endothelium, and this function is mediated in part by productive ligation of integrin α v β 3. (Penta[[,]] et al., "Del 1 induces integrin signaling and angiogenesis by ligation of α v β 3," *J. Biol Chem*, 16; 274 (April 1999)[[.]]).

Paragraph 30 beginning on page 10 has been amended as follows:

[0030] Nicotine, via stimulation of nicotinic receptors, has been shown to enhance angiogenesis and may stimulate tumor growth in part by enhancing tumor vascularity.

(Heesch et al., "Nicotine Stimulates Tumor Angiogenesis," Stanford University, Stanford, CA (2001)).

Paragraph 43 beginning on page 12 has been amended as follows:

[0043] The stent can be coated with a polymeric material for the delivery of the angiogenic substance alone or in combination with a therapeutic substance. "Polymer," "poly," and "polymeric" are defined as compounds that are the product of a polymerization reaction and are inclusive of homopolymers, copolymers, terpolymers etc., including random, alternating, block, and graft variations thereof. Representative examples of polymers that can be used with the embodiments of the present invention include ethylene vinyl alcohol copolymer (commonly known by the generic name EVOH or by the trade name EVAL); poly(hydroxyvalerate); poly(L-lactic acid); polycaprolactone; poly(lactide-co-glycolide); poly(hydroxybutyrate); poly(hydroxybutyrate-co-valerate); polydioxanone; polyorthoester; polyanhydride; poly(glycolic acid); poly(D,L-lactic acid); poly(glycolic acid-co-trimethylene carbonate); polyphosphoester; polyphosphoester urethane; poly(amino acids); cyanoacrylates; poly(trimethylene carbonate); poly(iminocarbonate); copoly(ether-esters) (e.g., PEO/PLA); polyalkylene oxalates; polyphosphazenes and biomolecules such as fibrin, fibrinogen, cellulose, starch, collagen and hyaluronic acid; polyurethanes; silicones; polyesters; polyolefins; polyisobutylene and ethylene-alphaolefin copolymers; acrylic polymers and copolymers; vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride and polyvinylidene chloride; polyacrylonitrile; polyvinyl ketones; polyvinyl aromatics, such as polystyrene; polyvinyl esters, such as polyvinyl acetate; copolymers of vinyl monomers with each other and olefins, such as ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins, and ethylene-vinyl acetate copolymers; polyamides, such as Nylon 66 and polycaprolactam; alkyl

resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins; polyurethanes; rayon; rayon-triacetate; cellulose; cellulose acetate; cellulose butyrate; cellulose acetate butyrate; cellophane; cellulose nitrate; cellulose propionate; cellulose ethers; and carboxymethyl cellulose.

Paragraph 52 beginning on page 17 has been amended as follows:

[0052] A suitable example of an antiproliferative substance is actinomycin D, or derivatives and analogs thereof. Synonyms of actinomycin D include dactinomycin, actinomycin IV, actinomycin I₁, actinomycin X₁, and actinomycin C₁. Examples of suitable antineoplastics include paclitaxel and docetaxel. Examples of suitable antiplatelets, anticoagulants, antifibrins, and antithrombins include sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogs, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist, recombinant hirudin, thrombin inhibitor (available from Biogen), and 7E-3B® (an antiplatelet drug from Centocore). Examples of suitable antimitotic agents include methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, adriamycin, and mitomycin. Examples of suitable cytostatic or antiproliferative agents include angiopeptin (a somatostatin analog from Ibsen), angiotensin converting enzyme inhibitors such as CAPTOPRIL (available from Squibb), CILAZAPRIL (available from Hoffman-LaRoche), or LISINOPRIL (available from Merck)[[;]], calcium channel blockers (such as Nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonist, LOVASTATIN (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug from Merck), monoclonal antibodies (such as PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available from Glaxo), Surmin (a PDGF antagonist), serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. Other

therapeutic substances or agents which may be appropriate include alpha-interferon, genetically engineered epithelial cells, and dexamethasone.